DEPARTMENT OF HEALTH AND HUMAN SERVICES

DEC 22 1994

Our Reference Nos: 93-1051 & 93-1057

John Parker, Ph.D.
Centocor B.V.
Einsteinweg 101
2333 CB Leiden, The Netherlands

Dear Dr. Parker

Enclosed is Department of Health and Human Services Establishment License No. 1178, issued to Centocor B.V., Leiden, The Netherlands, in accordance with the provisions of Title III Part F of the Public Health Service Act of July 1, 1944 (58 Stat. 702) controlling the manufacture and sale of biological products. This license authorizes you to manufacture and import into this country for sale, barter, or exchange those products for which your establishment holds unsuspended and unrevoked product licenses issued by the Department of Health and Human Services.

Also enclosed is a product license authorizing your establishment to manufacture and ship for sale, barter, or exchange in interstate and foreign commerce, Abciximab, to be manufactured in 5 ml fill size by Centocor B.V. and distributed by Eli Lilly and Company under the trade name ReoPro. Abciximab is approved for use as an adjunct to percutaneous transluminal coronary angioplasty or atherectomy (PTCA) for the prevention of acute cardiac ischemic complications in patients at high risk for abrupt closure of the treated coronary vessel.

You are requested to submit samples of each future lot of the product together with protocols showing results of all applicable tests. No lots of product shall be distributed until notification of release is received from the Director, Center for Biologics Evaluation and Research.

The dating period for the dosage formulation of this product shall be 30 months from the date of manufacture when stored at 2-8°C. The date of manufacture shall be defined as the date of the final sterile filtration of the bulk. The preformulated bulk may be stored for up to ——— at ——— Results of ongoing stability studies should be submitted throughout the dating period as they become available including the results of stability studies from the first three commercial production lots.

We acknowledge the written commitments to conduct clinical studies and make manufacturing changes as specified in your letters of October 26, December 9, December 14, and December 20, 1994. These commitments include:

1. Post-marketing clinical studies to address the effects of modifications to the therapeutic regimen on bleeding risk and efficacy, the effects of platelet transfusions in Abciximab-treated patients, and the readministration of Abciximab;

2. Monitoring the occurrence of intracranial hemorrhage and stroke in Abciximab-treated patients; and

3. Modifications to the stability protocol and manufacturing facility.

It is requested that adverse experience reports be submitted in accordance with the adverse experience reporting requirements for licensed biological products (21 CFR 600.80) and that distribution reports be submitted as described (21 CFR 600.81). These requirements become effective on December 27, 1994. All experience reports should be prominently labeled according to 21 CFR 600.80 and be submitted to Center for Biologics Evaluation and Research, HFM-210, Food and Drug Administration, 1401 Rockville Pike, Rockville, MD, 20852-1448.

Please submit three copies of final printed labeling at the time of use and include Part II of the label transmittal form with completed implementation information. In addition, advertising and promotional labeling should be submitted for review and approval prior to the initial publication of any advertisement and prior to the initial dissemination of any promotional labeling for the first 120 days following approval. All promotional claims must be consistent with and not contrary to approved labeling. No comparative promotional claim or claim of superiority over other similar products should be made unless data to support such claims are submitted to and approved by the Center for Biologics Evaluation and Research.

It is requested that you acknowledge receipt of the enclosed product license to the Director, Division of Application Review and Policy, HFM-585, and the enclosed establishment license to the Director, Division of Establishment Licensing, HFM-205, Center for Biologics Evaluation and Research.

Sincerely yours,

Jerome A. Donlon, M.D., Ph.D.
Director
Office of Establishment Licensing
and Product Surveillance
Center for Biologics
Evaluation and Research

Kenneth B. Seamon, Ph.D.
Acting Director
Office of Therapeutics
Research and Review
Center for Biologics
Evaluation and Research

Enclosures

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